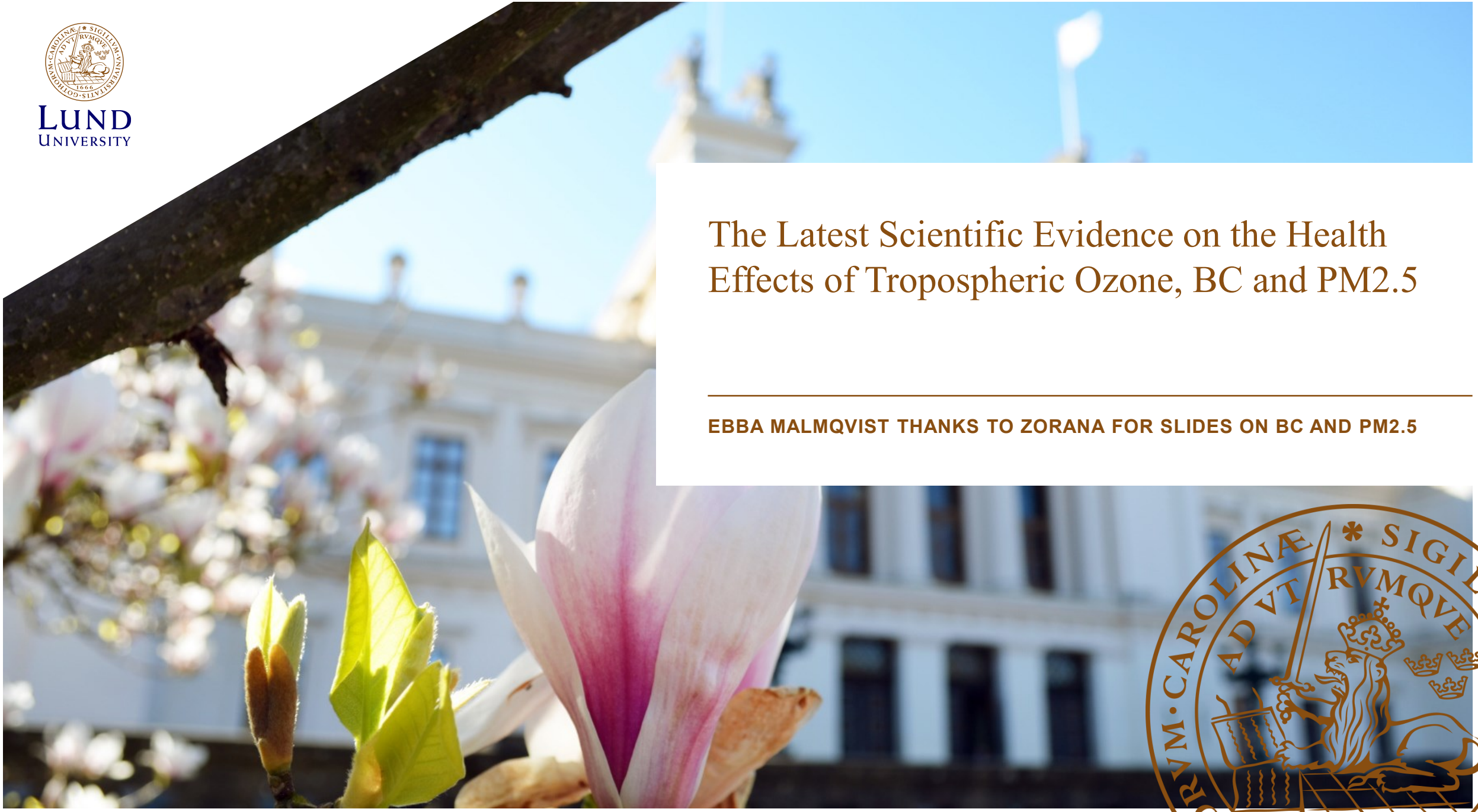
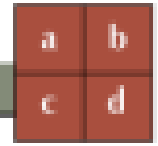


The Latest Scientific Evidence on the Health Effects of Tropospheric Ozone, BC and PM2.5

EBBA MALMQVIST THANKS TO ZORANA FOR SLIDES ON BC AND PM2.5

Relative Risk (RR)



Relative risk is a ratio of an event:

persons **exposed** ▪ persons **unexposed**

$$\frac{\text{Incidence in the exposed}}{\text{Incidence in the non-exposed}}$$

The larger the relative risk, the stronger the evidence for a causal relationship.

Large relative risk alone does not prove a causal relationship.

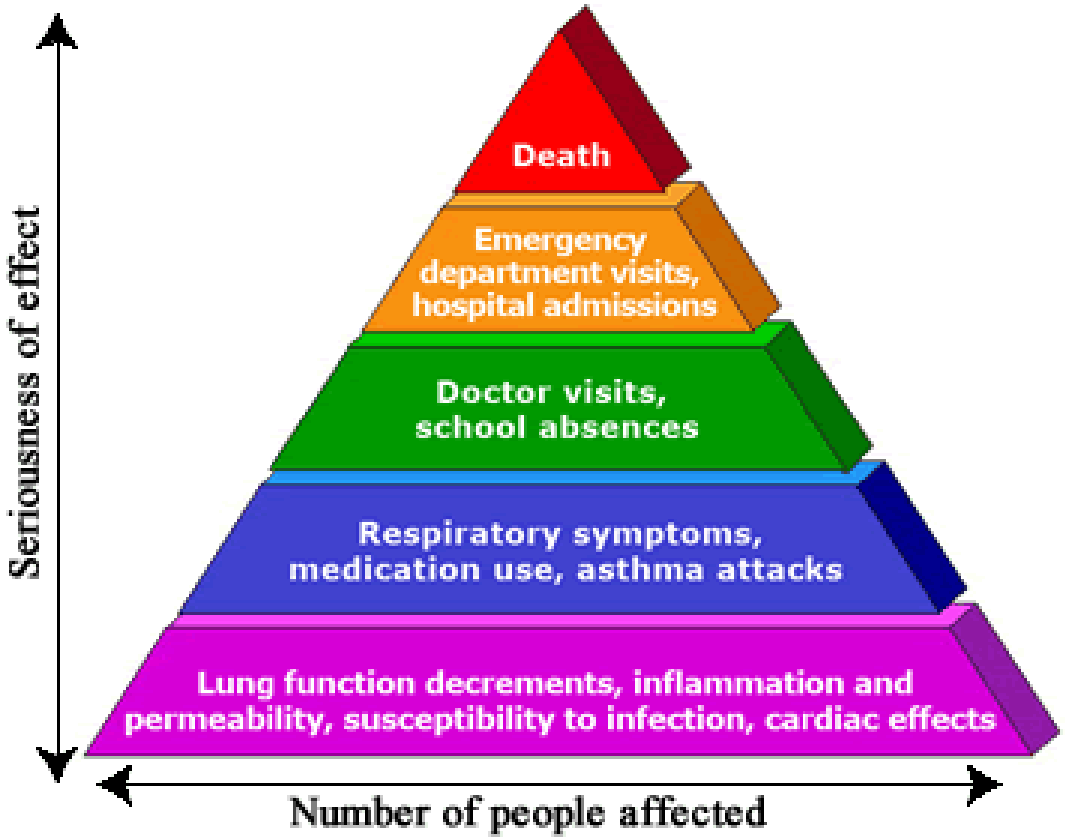
RR = 1: no evidence of an association

RR > 1: exposure is harmful

RR < 1: exposure may be protective

For an introduction to causality, see the module Cause and Effect in Epidemiology.

Pyramid of effects caused by air pollution



US EPA
2024

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Causality steps

The five categories are:

- causal relationship;
- likely to be a causal relationship;
- suggestive of, but not sufficient to infer, a causal relationship;
- inadequate to infer the presence or absence of a causal relationship; and
- not likely to be a causal relationship.

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(EMAPEC) WHO

Meta-analysis

ISEE Environmental Epidemiology

OPEN

Choices of morbidity outcomes and concentration–response functions for health risk assessment of long-term exposure to air pollution

Francesco Forastiere[a,b,*], Joseph V. Spadaro[c,d], Carla Ancona[e], Zorana Jovanovic Andersen[f], Ilaria Cozzi[e], Sophie Gumy[c], Dejan Loncar[c], Pierpaolo Mudu[g], Sylvia Medina[h], Roman Perez Velasco[g], Heather Walton[b,i], Jiawei Zhang[f], Michal Krzyzanowski[b]

Table 2.

Relative risk estimates for incidence of diseases from selected systematic reviews recommended for health risk assessment of $PM_{2.5}$ and NO_2

Outcome (incidence)	ICD-10 codes	Age (yrs)	List	RR (95% CI) per 10 μg/m³	Mean exposure range (μg/m³)	SR reference
Long-term exposure to $PM_{2.5}$						
Asthma in children	J45	0–18	A	1.34 (1.10, 1.63)	5–38	Khreis et al[37]
COPD	J41–J44	30+	A	1.18 (1.13, 1.23)	5–26	Park et al[38]
IHD events[a]	I21–I22	30+	A	1.13 (1.05, 1.22)[b]	5–65	Zhu et al[39]
Stroke	I60–I64	30+	A	1.16 (1.12, 1.20)[b]	5–36	Yuan et al[40]
Hypertension	I10–I11	30+	A	1.17 (1.05, 1.30)[b]	5–77	Qin et al[41]
Diabetes (type 2)	E11–E14	30+	B+	1.10 (1.03, 1.18)[b]	5–79	Yang et al[42]
Dementia	F00–F03, G30	60+	B+	1.46 (1.20, 1.78)[b]	5–25[c]	Cheng et al[43]
ASD	F84.0, F84.1, F84.5, F84.8, F84.9	2–12	B+	1.66 (1.23, 2.25)[b]	5–30[c]	Lin et al[44]
Lung cancer	C34	30+	A	1.16 (1.10, 1.23)	5–44	Yu et al[36]
Long-term exposure to NO_2						
Asthma in children	J45	0–18	A	1.10 (1.05, 1.18)	10–39	Khreis et al[37]
Asthma in adults	J45	19+	A	1.10 (1.01, 1.21)	10–40	HEI[34]
ALRI in children	J12–J18, J20–J22	0–12	A	1.09 (1.03, 1.16)	10–56	HEI[34]

[a]Acute myocardial infarction (AMI).

[b]Relative risk estimates from revised meta-analysis.

[c]Restrict applicability of the CRFs of these conditions to exposure differences not larger than 10 μg/m³ within the indicated concentration ranges (see discussion in eAppendix 2; http://links.lww.com/EE/A280).

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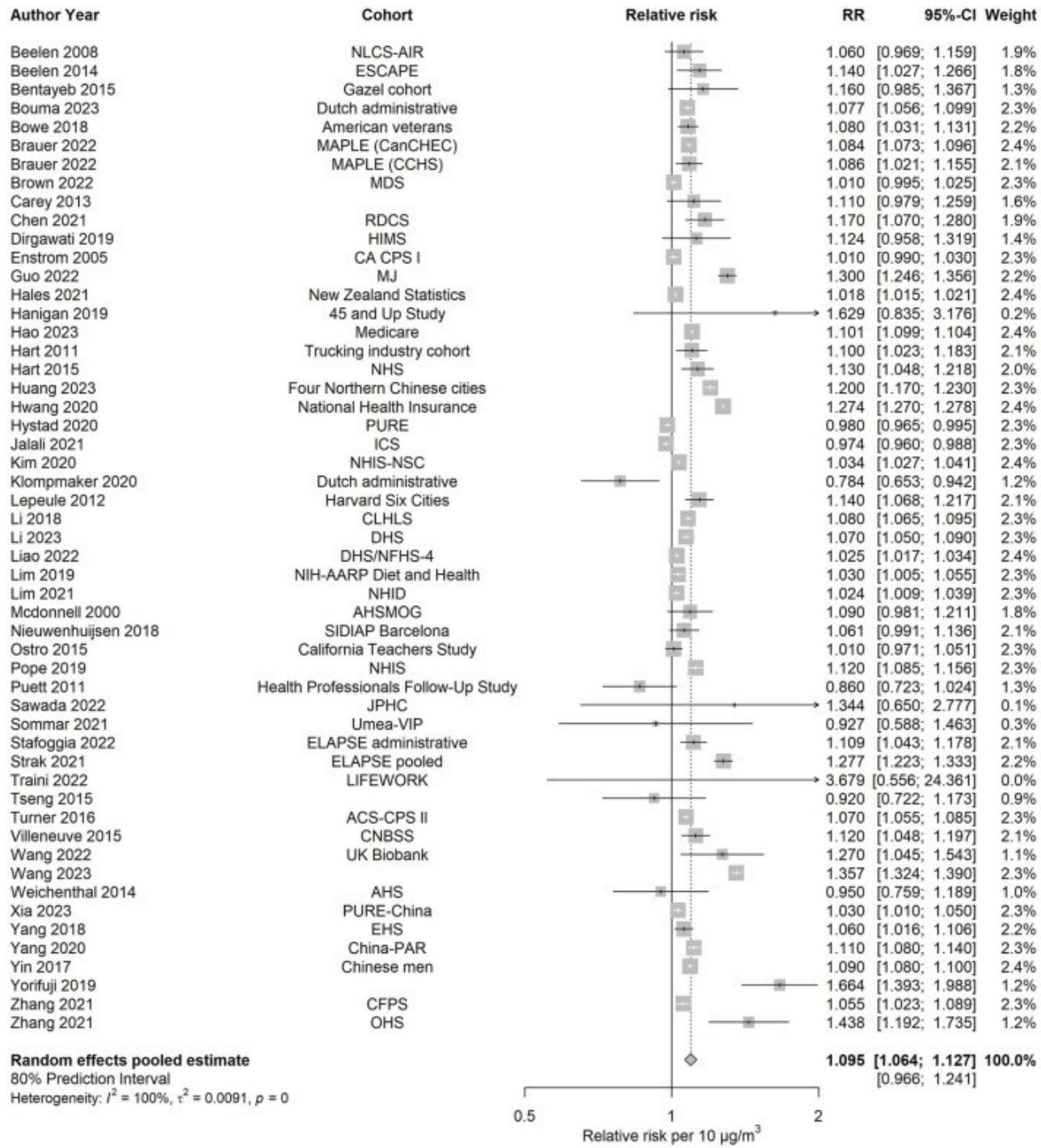
https://www.who.int/activities/estimating-the-morbidity-from-air-pol-lution-and-its-economic-costs.

Mortality-$PM_{2.5}$ 2024 meta-analyses WHO HRAPIE-2

- WHO HRAPIE-2 Project
- Orellano, 2024
- 53 studies
- RR = 1.095 (1.06-1.13)



https://pmc.ncbi.nlm.nih.gov/articles/PMC11466858/pdf/ijph-69-1607683.pdf

Development of RRs mortality and long-term PM2.5 per 10 µg/m3)

- HRAPIE (Hoek 2013) 1.062 (1.040-1.082)
- WHO 2021 AGQ (Chen&Hoek 2020) 1.080 (1.040-1.090)
- ELAPSE (Hoffmann 2022) 1.119 (1.060-1.179)
- HAPIE-2 (Orellano 2024) 1.095 (1.064-1.227)

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Conclusions: recommended CRFs for health impacts

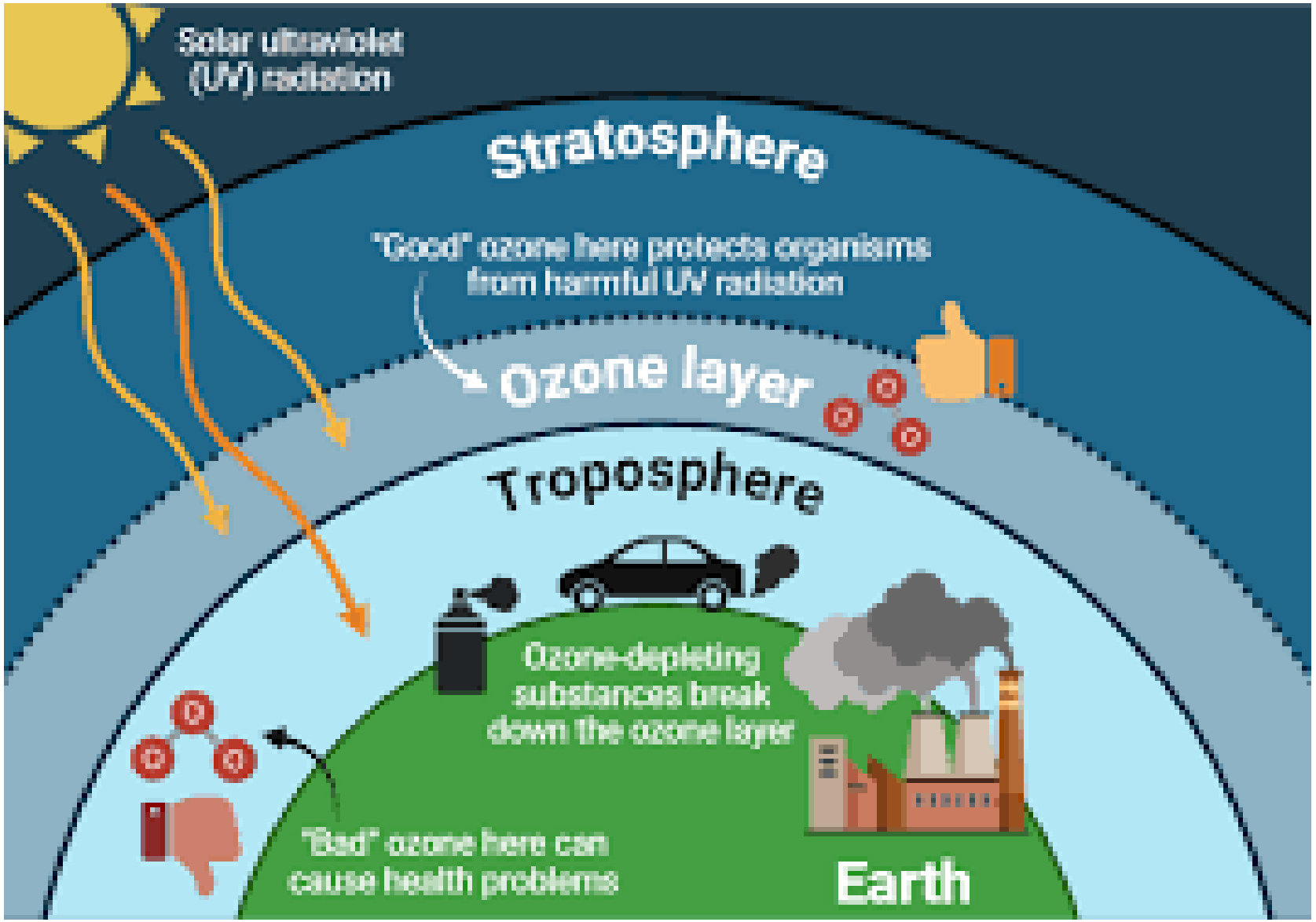
Mortality: HRAPIE-2 Project WHO

- **$PM_{2.5}$ RR = 1.095 (Orellano 2024)**
- **NO_2 RR= 1.045 (Kasdagli 2024)**
- **Sensitivity analyses European ELAPSE (Hoffmann, 2022) $PM_{2.5}$ RR = 1.12 & NO_2 RR= 1.04**

Morbidity: EMAPEC Project WHO (Forastiere, 2024)

- **$PM_{2.5}$ & NO_2**

What about ozone?



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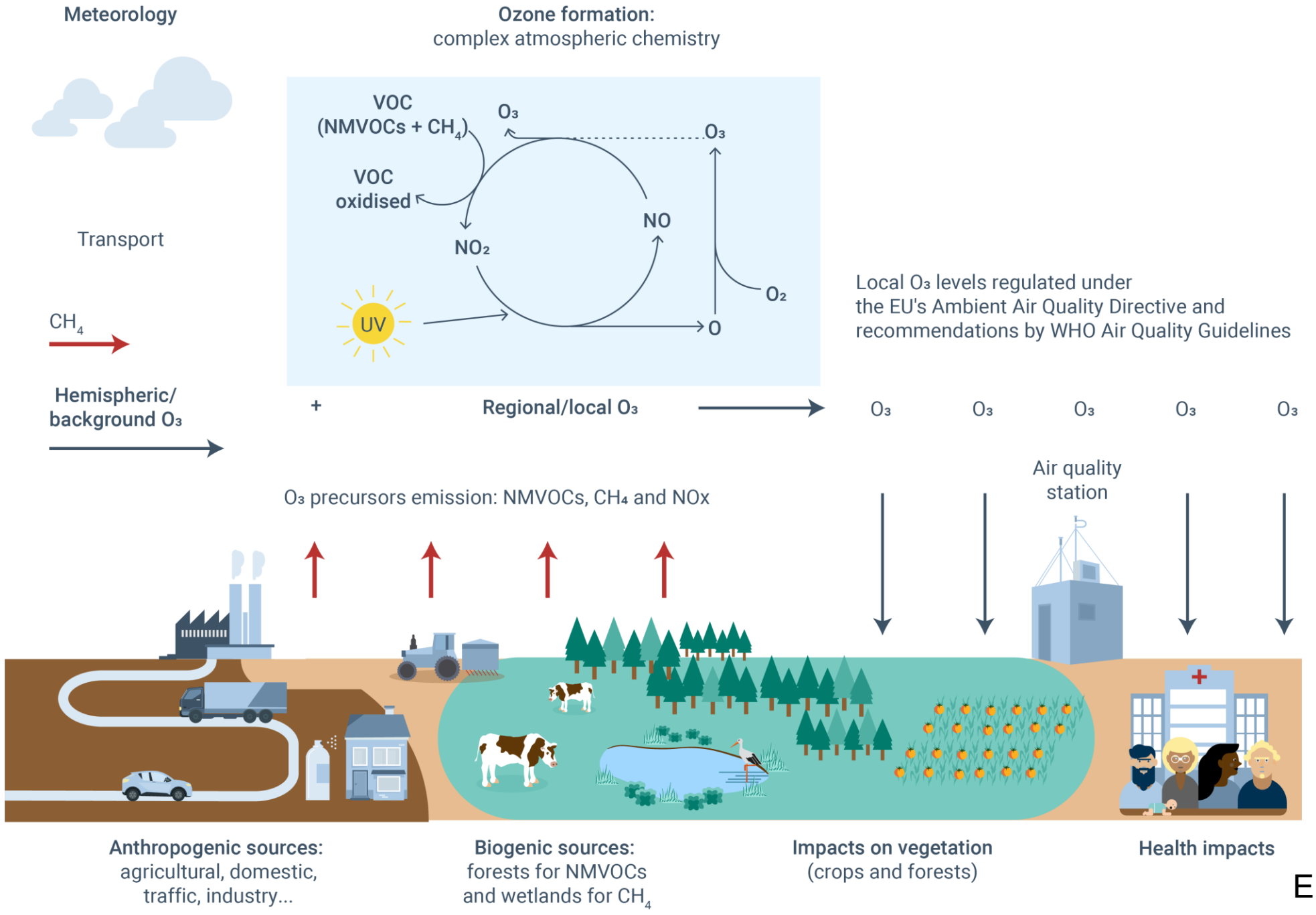
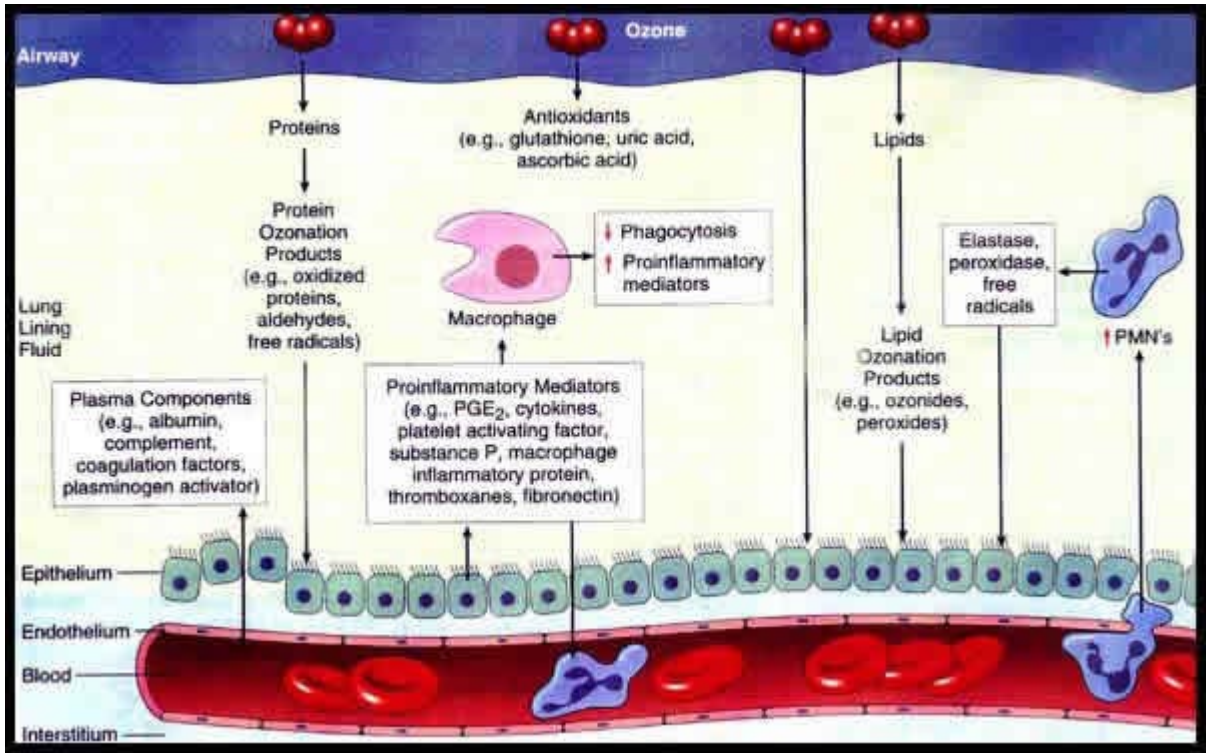

Meteorology
Ozone formation:
complex atmospheric chemistry
VOC
(NMVOCs + CH4)
O3
O3
VOC
oxidised
NO
NO2
O2
UV
O
Transport
CH4
Local O3 levels regulated under
the EU's Ambient Air Quality Directive and
recommendations by WHO Air Quality Guidelines
Hemispheric/
background O3
+
Regional/local O3
O3
O3
O3
O3
O3
Air quality
station
O3 precursors emission: NMVOCs, CH4 and NOx
Anthropogenic sources:
agricultural, domestic,
traffic, industry...
Biogenic sources:
forests for NMVOCs
and wetlands for CH4
Impacts on vegetation
(crops and forests)
Health impacts

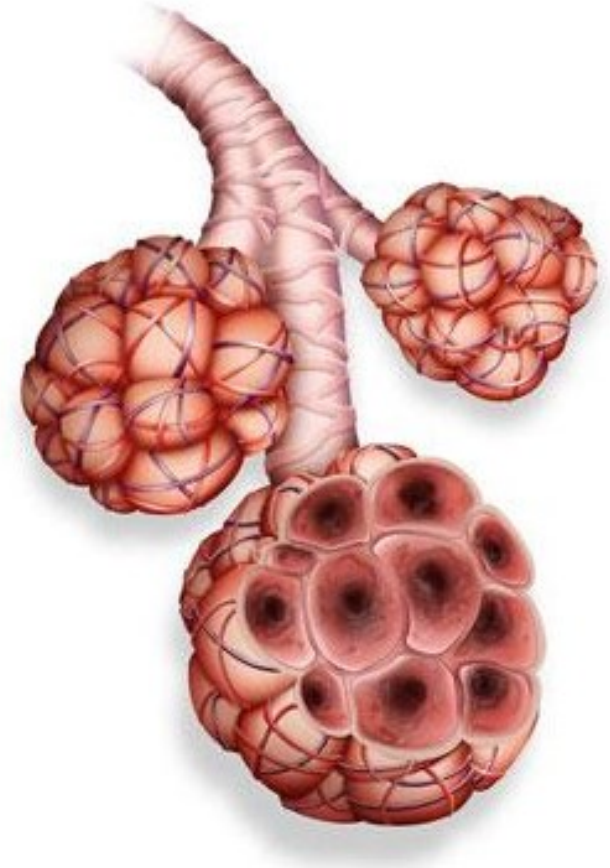
EEA, 2023

Biological mechanisms



Ozone is highly reactive in the respiratory tract Devlin et al., (1997)

US EPA 2017



Ozone can cause the muscles in the airways to constrict, trapping air in the alveoli. This leads to wheezing and shortness of breath.

Table ES-1 Summary of causality determinations by exposure duration and health outcome.

Health Outcome[a]	Conclusions from 2013 Ozone ISA	Conclusions in the 2020 ISA
Short-term exposure to ozone		
Respiratory effects	Causal relationship	Causal relationship
Cardiovascular effects	Likely to be causal relationship	Suggestive of, but not sufficient to infer, a causal relationship[c]
Metabolic effects	No determination made	Likely to be causal relationship[b]
Total mortality	Likely to be causal relationship	Suggestive of, but not sufficient to infer, a causal relationship[c]
Central nervous system effects	Suggestive of a causal relationship[d]	Suggestive of, but not sufficient to infer, a causal relationship
Long-term exposure to ozone		
Respiratory effects	Likely to be causal relationship	Likely to be causal relationship
Cardiovascular effects	Suggestive of a causal relationship[d]	Suggestive of, but not sufficient to infer, a causal relationship
Metabolic effects	No determination made	Suggestive of, but not sufficient to infer, a causal relationship[b]
Total mortality	Suggestive of a causal relationship[d]	Suggestive of, but not sufficient to infer, a causal relationship
Reproductive effects	Suggestive of a causal relationship[d]	Effects on fertility and reproduction: suggestive of, but not sufficient to infer, a causal relationship[b]
		Effects on pregnancy and birth outcomes: suggestive of, but not sufficient to infer, a causal relationship[b]
Central nervous system effects	Suggestive of a causal relationship[d]	Suggestive of, but not sufficient to infer, a causal relationship
Cancer	Inadequate to infer a causal relationship	Inadequate to infer the presence or absence of a causal relationship[e]

[a]Health effects (e.g., respiratory effects, cardiovascular effects) include the spectrum of outcomes, from measurable subclinical effects (e.g., decrements in lung function, blood pressure) to observable effects (e.g., medication use, hospital admissions) and cause-specific mortality. Total mortality includes all-cause (nonaccidental) mortality, as well as cause-specific mortality.

[b]Denotes new causality determination.

[c]Denotes change in causality determination from 2013 Ozone ISA.

[d]Since the 2013 Ozone ISA, the causality determination language has been updated and this category is now stated as suggestive of, but not sufficient to infer, a causal relationship.

[e]Since the 2013 Ozone ISA, the causality determination language has been updated and this category is now stated as inadequate to infer the presence or absence of a causal relationship.

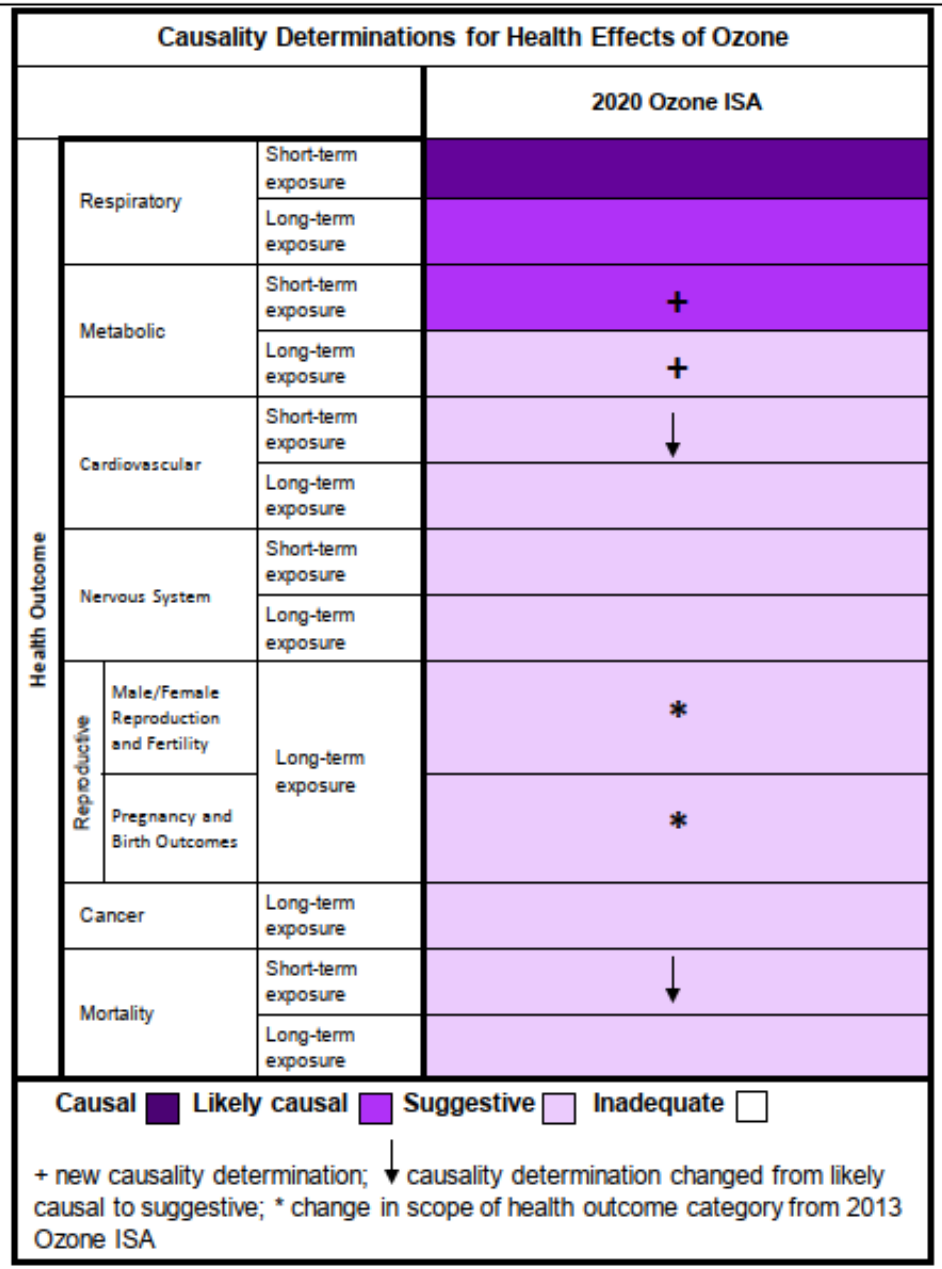


Figure ES-2 Causality determinations for health effects of short- and long-term exposure to ozone.

US EPA 2020

Proceedings for the Ozone Workshop US EPA 2024

Emerging research areas/findings include impact on the brain.

Increase in studies on COPD and other respiratory diseases.

In general, more linear concentration-response functions on short-term effects with no threshold.

Short-term effects of O3 exposure, lag of one or two days for respiratory endpoints and had a lag of up to five days for cardiovascular endpoints.

Recent meta-analysis

TABLE 2 | Meta-analysis results and characteristics of studies informing the associations between long-term exposure to ozone (O_3) (per 10 μg/m^3 increase) and mortality outcomes (Global, 2023-2024).

A) Annual O_3

	N	RR (95% CI)	I^2 (%)	80% prediction interval	Sample size	Age (years)	Median of O_3 (min – max)
All-cause	9	1.01 (0.96, 1.06)	92	(0.91, 1.11)	1,622,831	>30	60.6 (42.3–94.3)
Respiratory disease	6	1.05 (1.02,1.08)	65	(1.00, 1.09)	1,544,274	>30	70.4 (50.8–94.3)
COPD	2	1.06 (1.03, 1.08)	25	-	1,217,826	>30	74.87–76.44*
ALRI	2	1.04 (0.97, 1.11)	80	-	1,217,826	>30	74.87–76.44*

B) Peak/warm season O3

	N	RR (95% CI)	I^2 (%)	80% Prediction Interval	Sample size	Age (years)	Median of O_3 (min – max)
All-cause	12	1.01 (0.97, 1.04)	98	(0.92, 1.10)	107,896,036	>18	90.6 (74.9–106.6)
Respiratory disease	9	1.01 (0.98, 1.03)	92	(0.95, 1.06)	57,107,136	>25	85 (74.9–109.8)
COPD	7	1.00 (0.96, 1.04)	95	(0.92, 1.09)	56,668,296	>25	85 (74.9–109.8)
ALRI	4	1.02 (0.99, 1.04)	88	(0.97, 1.07)	23,702,383	>30	87.9 (74.9–109.8)

N = number of studies; min: minimum; max: maximum.

Kaudagli et al, 2024

What about BC?

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2nd Global Conference on Air Pollution and Health

Overview of exposure and health effects of black carbon, evidence gaps

Session number: 7c
Bridging Air Pollution, Health and Climate: Tackling Black Carbon and Ultrafine Particles
March 26 / 14:30-16:00

Zorana Jovanovic Andersen */ Professor in Environmental Epidemiology, University of Copenhagen, Denmark; Former Chair of ERS Environment and Health Committee*

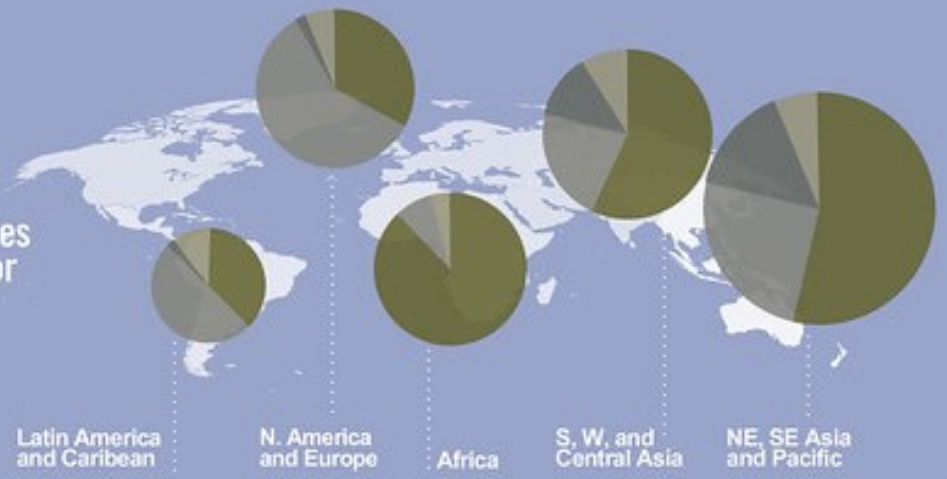
Black Carbon (BC)
and Co-pollutants from Incomplete Combustion

Black carbon particles are formed from the incomplete combustion of biomass and fossil fuels. It is a powerful climate forcer and dangerous air pollutant.

Days

EMISSIONS

Main BC-rich sources by region and sector (2005)



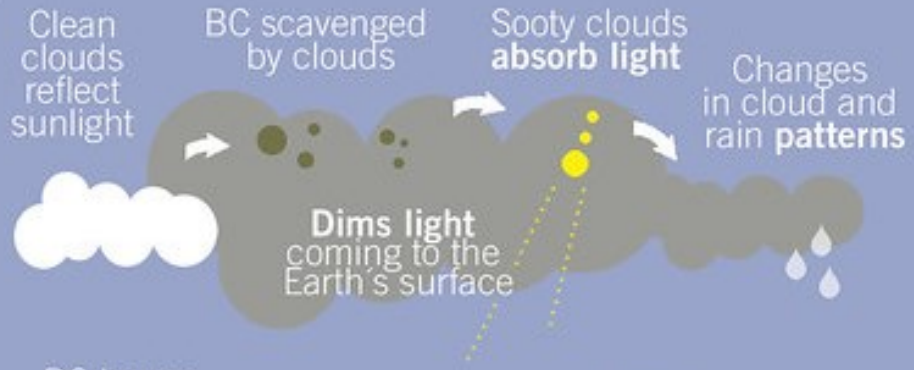
PRIMARY BLACK CARBON-RICH SOURCES

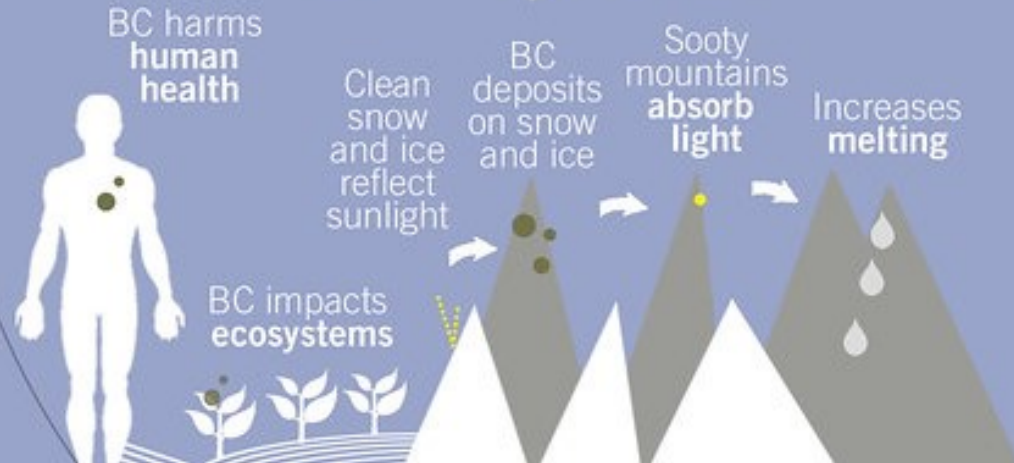
BC is always emitted with co-pollutant particles, some of which have a cooling effect on climate. The ratio of BC to co-pollutants varies by source and determines if a measure has a **net warming or net cooling effect.**

IMPACTS

Suspended in the atmosphere, BC particles contribute to **global warming** by absorbing energy and converting it to heat

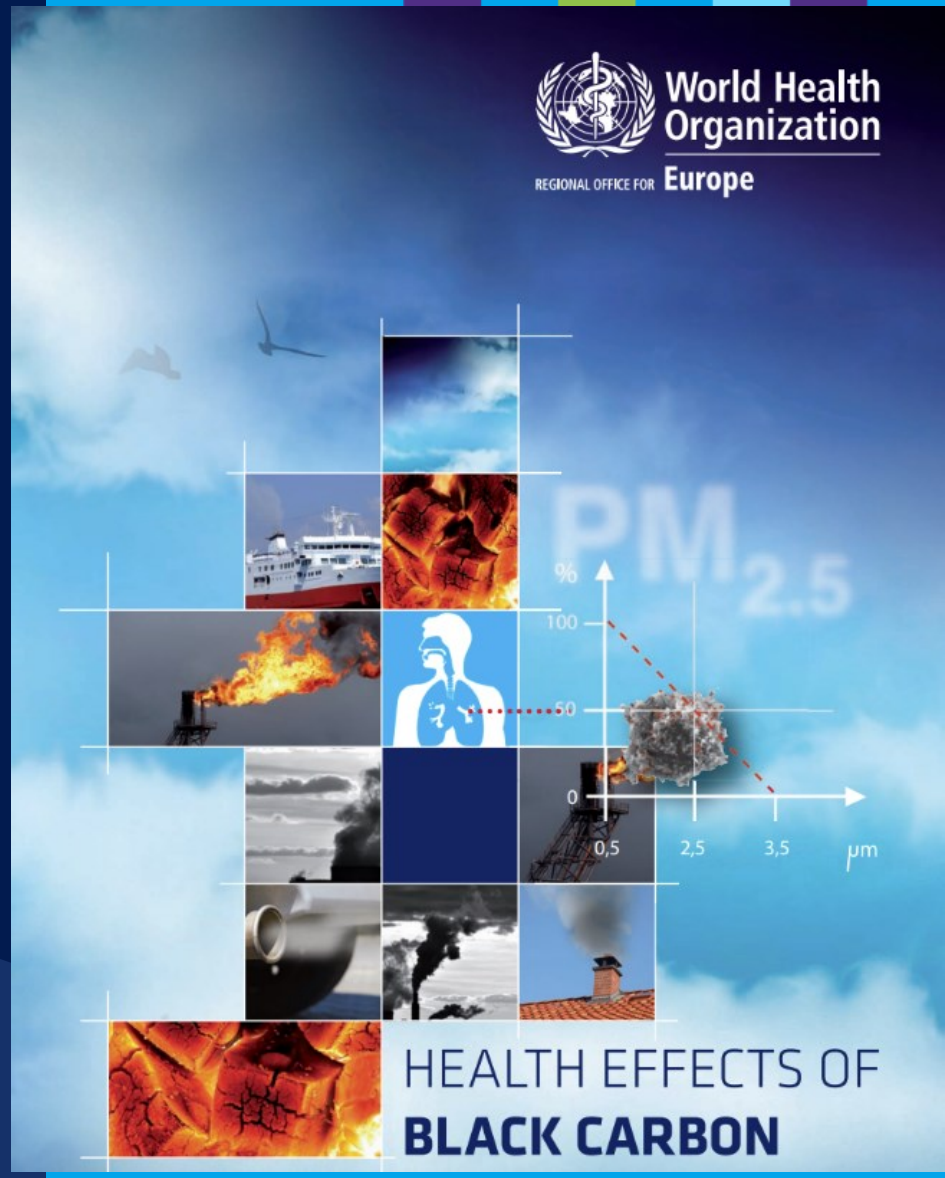
BC is a dangerous local air pollutant which can also be **transported across the globe**





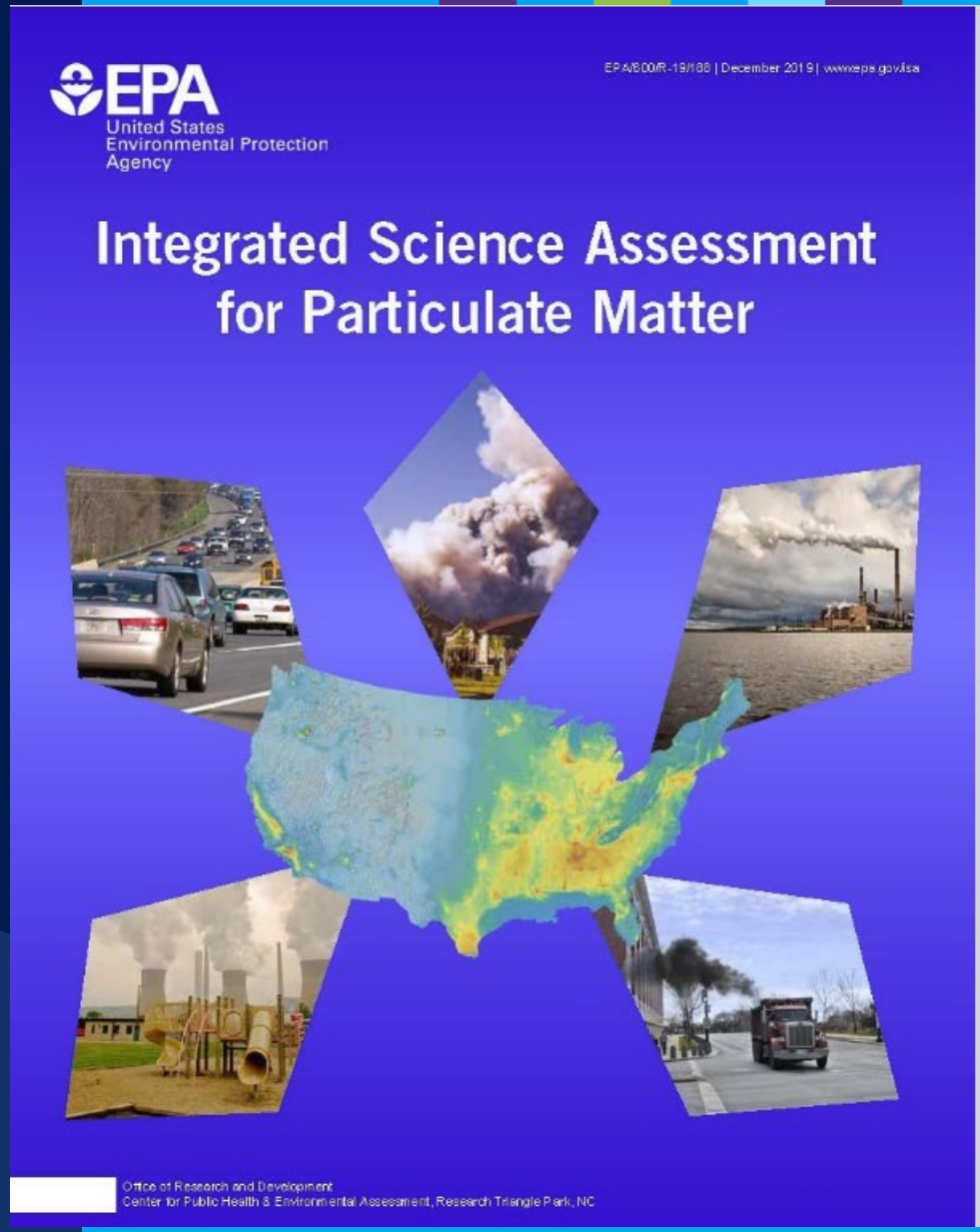
Health Effects of Black Carbon: WHO (2012)

- Sufficient evidence on association of short-term exposure to BC and health (all-cause and CVD mortality, cardiopulmonary hospital admissions)
- The evidence from long term studies is inconclusive in multi-pollutant models.
- Effects estimates (from both short- and long-term studies) are much higher for BC compared to PM10 and PM2.5 when the particulate measures are expressed per unit of mass concentration (µg/m3).
- There are not enough clinical or toxicological studies to allow an evaluation of the qualitative differences between the health effects of exposure to BC or to PM mass
- BC may be useful as an additional indicator in evaluating local action aimed at reducing the population exposure to combustion PM (from motorized traffic)
- The Task Force on Health recommends to continue using $PM_{2.5}$ as the primary metric in quantifying exposure to PM and its health effects , and for predicting benefits of reduction measures



Health Effects of Black Carbon. EPA (2019)

- **EPA Integrated Science Assessment for Particulate Matter (2019):** 'PM Components and Sources: Many $PM_{2.5}$ components and sources are associated with many health effects, and the evidence does not indicate that any one source or component is more strongly related with health effects than $PM_{2.5}$ mass…'



Health Effects of Black Carbon: WHO Air Quality Guideline (2021)

Box 4.1. Good practice statement – BC/EC

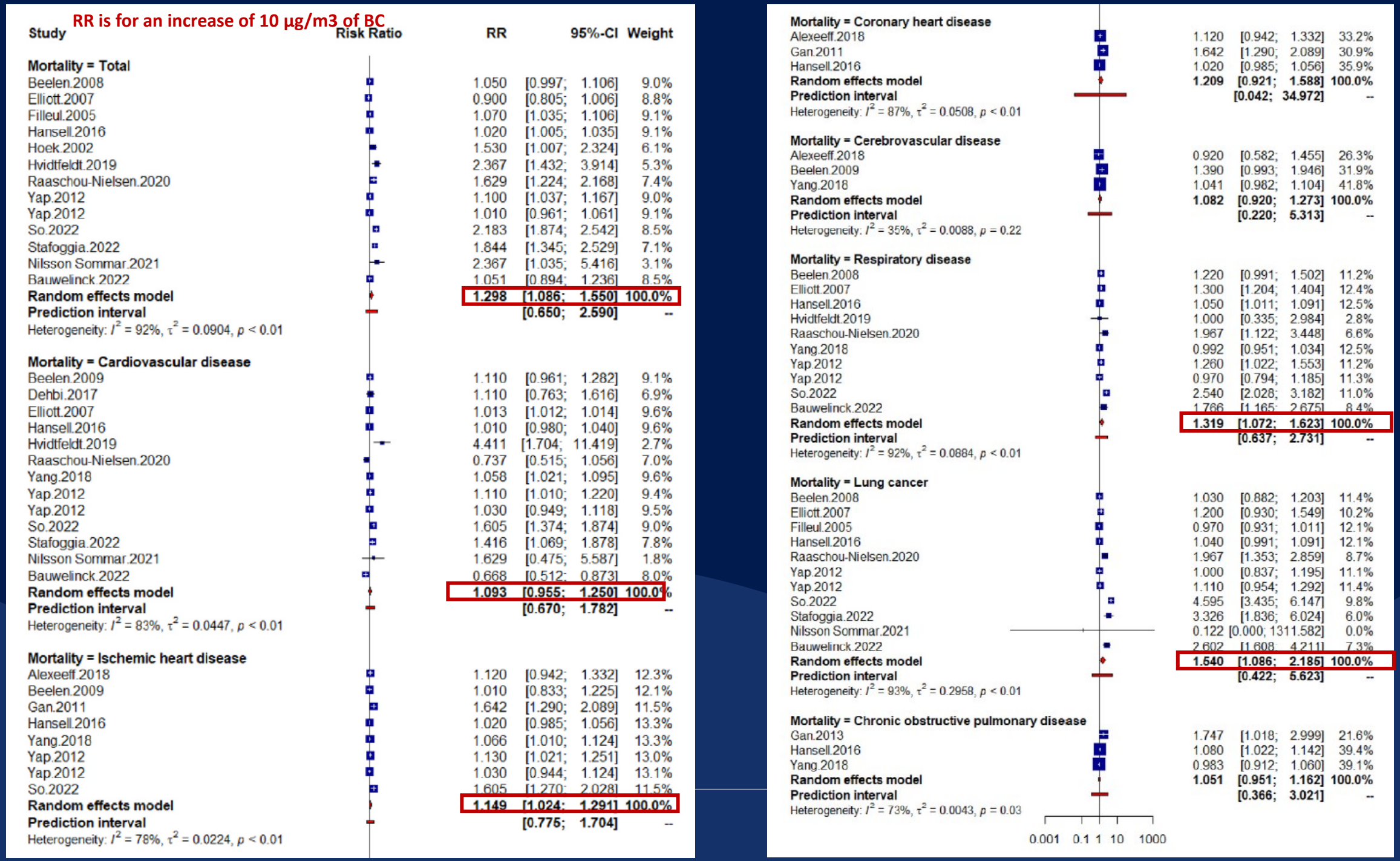
Based on insufficient evidence to propose an AQG level, the GDG decided to formulate the following three good practice statements on BC/EC directed to countries and regional authorities.

1. Make systematic measurements of black carbon and/or elemental carbon. Such measurements should not replace or reduce the existing monitoring of pollutants for which guidelines currently exist.
2. Undertake the production of emission inventories, exposure assessments and source apportionment for BC/EC.
3. Take measures to reduce BC/EC emissions from within the relevant jurisdiction and, where considered appropriate, develop standards (or targets) for ambient BC/EC concentrations.

BC: review of epidemiological evidence: long-term exposure to BC and mortality

- Zhu X, et al. Short and long-term association of exposure to ambient black carbon with all-cause and cause-specific mortality: A systematic review and meta-analysis. Environ Pollut. **2023** May 1;324:121086.

RR is for an increase of 10 µg/m3 of BC



BC: review of epidemiological evidence: long-term exposure to BC and mortality

New studies after meta analysis:

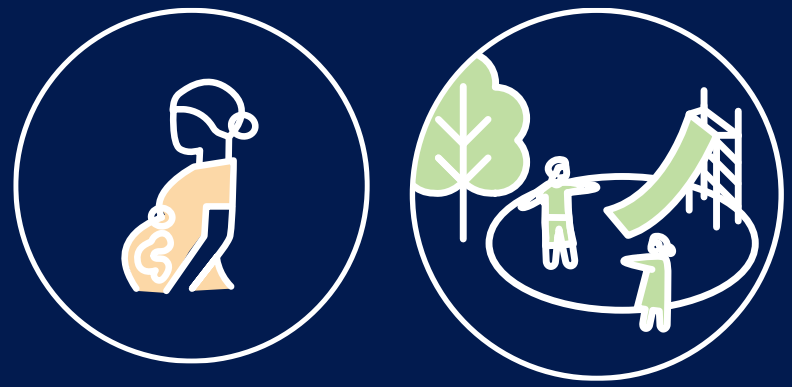
1. Zhu A, et al. Black Carbon Air Pollution and Incident Mortality Among the Advance-Aged Adults in China: A Prospective Cohort Study. J Gerontol A Biol Sci Med Sci. **2025**;80(4):glae302.
2. Weichenthal S, et al. Long-Term Exposure to Outdoor Ultrafine Particles and Black Carbon and Effects on Mortality in Montreal and Toronto, Canada. Res Rep Health Eff Inst. **2024**;2024:217.
3. Olstrup H, et al. The Long-Term Mortality Effects Associated with Exposure to Particles and NOx in the Malmö Diet and Cancer Cohort. Toxics. **2023**;11(11):913.

Long-term exposure to black carbon and all-cause mortality: is effect of BC independent of that of $PM_{2.5}$?

Reference	Location	Study design / cohort name	Hazard ratio (95% CI) for BC	$PM_{2.5}$ adjustment
Zhu et al. 2025	China (very old population)	Cohort study (CLHLS)	1.39 (1.36, 1.43), 1 μg/m^3	3.10 (2.94, 3.26)
Weichenthal et al. 2024	Montreal and Toronto, Canada	Cohort study (CanCHEC)	1.03 (1.03, 1.04), 0.5 μg/m^3	1.009 (1.004, 1.015) ($PM_{2.5}$ and O_x)
Olstrup et al. 2023	Malmö, Sweden	Cohort study (MDC)	1.05 (1.02, 1.08), 0.15 μg/m^3	1.05 (1.02, 1.09)
So et al. 2022	Denmark	Cohort study (administrative)	**1.05** (1.04, 1.06), 0.5 μg/m^3	**1.03** (1.02, 1.04)
Stafoggia et al. 2022	European multi-countrywide	Cohort study (ELAPSE administrative cohorts)	**1.04** (1.02, 1.06), 0.44 μg/m^3	**1.03** (1.01, 1.05)
Bauwelinck et al. 2022	Belgium	Cohort study (administrative)	1.00 (1.00, 1.00), 0.44 μg/m^3	0.99 (0.99, 1.00)
			1.00 (1.00, 1.01), 0.44 μg/m^3	1.01 (1.00, 1.01)
Strak et al. 2021	European mulit-cohort	Cohort study (ELAPSE pooled cohorts)	**1.08** (1.06, 1.10), 0.44 μg/m^3	**1.04** (1.02, 1.06)
Raschou-Nielsen et al. 2020	Denmark	Case-control (administrative cohort)	**1.05** (1.02, 1.08), 1 μg/m^3	**1.04** (1.01, 1.07)

BC and morbidity: long-term exposure to black carbon during pregnancy and maternal and fetal health

CHILD:
- Low birthweight (7 studies +, one-)
- Preterm birth (2 studies +, one-)
- Asthma incidence (one study +)
- Childhood wheeze (one study +)
- Hay fever and allergic rhinitis (one study +)
- Newborn systolic blood pressure (two studies +)
- Total fat mass, newborn insulin resistance (one study +)



MOTHER:
- Gestational diabetes melliuts (GDM) (one study +)
- Impaired glucose tolerance (IGT) (one study +)
- Preeclampsia (one study+)

* Goriainova V, et al. Adverse Effects of Black Carbon (BC) Exposure during Pregnancy on Maternal and Fetal Health: A Contemporary Review. Toxics. **2022**;10(12):779 Sinsamala RM, et al. Pregnancy outcomes as related to in utero exposure to air pollution and greenness: The Life-GAP Project. Environ Epidemiol. 2024;8(4):e318; Dong S, et al. Maternal exposure to black carbon and nitrogen dioxide during pregnancy and birth weight: Using machine-learning methods to achieve balance in inverse-probability weights. Environ Res. 2022;211:112978.

Conclusion

- New ERFs for PM2.5 both mortality and morbidity
- Health effects also on long term exposure of ozone
- The evidence base on BC is increasing (new WHO report end of year)

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THANKS FOR LISTENING!
ACKNOWLEDGING ALL THE PEOPLE BEHIND THE RESEARCH